

***IN THE UNITED STATES PATENT AND TRADEMARK OFFICE***

Applicant: Peng Cho TANG et al.  
Title: BICYCLIC PROTEIN KINASE INHIBITORS  
Prior Appl. No.: 09/819,698  
Prior Appl. Filing Date: 03/29/2001  
Examiner: Unassigned  
Art Unit: Unassigned

**INFORMATION DISCLOSURE STATEMENT**  
**UNDER 37 CFR §1.56**

Mail Stop PATENT APPLICATION  
Commissioner for Patents  
PO Box 1450  
Alexandria, Virginia 22313-1450

Sir:

Applicants submit herewith on Form PTO/SB/08 a listing of the documents cited by or submitted to the U.S. PTO in parent application Serial No. 09/819,698, filed 03/29/2001, which is a divisional of application Serial No. 09/074,621, filed 05/07/1998. As provided in 37 CFR §1.98(d), copies of the documents are not being provided since they were previously submitted to the United States Patent & Trademark Office in the above-identified parent applications.

The submission of any document herewith, which is not a statutory bar, is not intended as an admission that such document constitutes prior art against the claims of the present application or that such document is considered material to patentability as defined in 37 CFR §1.56(b). Applicants do not waive any rights to take any action which would be appropriate to antedate or otherwise remove as a competent reference any document which is determined to be a *prima facie* art reference against the claims of the present application.

**TIMING OF THE DISCLOSURE**

The listed documents are being submitted in compliance with 37 CFR §1.97(b), within three (3) months of the filing date of the application.

Applicants respectfully request that the listed document be considered by the Examiner and be made of record in the present application and that an initialed copy of Form PTO/SB/08 be returned in accordance with MPEP §609.

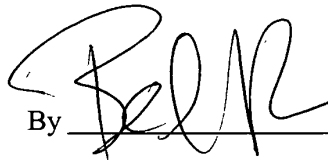
The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 CFR §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741.

Respectfully submitted,

Date

12/2/03

By



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Beth A. Burrous

Attorney for Applicant

Registration No. 35,087

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				First Named Inventor	Peng Cho TANG
				Group Art Unit	Unassigned
				Examiner Name	Unassigned
				Attorney Docket Number	034536-0906
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U.S. PATENT DOCUMENTS						
Examiner Initials*	Cite No. <sup>1</sup>	U.S. Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number	Kind Code <sup>2</sup> (if known)			
	A1	Re. 36,256	E	Spada et al.	07-20-1999	
	A2	4,002,749		Rovnyak	01-11-1977	
	A3	4,053,613		Rovnyak et al.	10-11-1977	
	A4	4,966,849		Vallee et al.	10-30-1990	
	A5	5,196,446	A	Levitzki et al.	03-23-1993	
	A6	5,217,999	A	Levitzki et al.	06-08-1993	
	A7	5,302,606	A	Spada et al.	04-12-1994	
	A8	5,322,950	A	Sircar et al.	06-21-1994	
	A9	5,330,992	A	Eissenstat et al.	07-19-1994	
	A10	5,397,787	A	Buzzetti et al.	03-14-1995	
	A11	5,786,488	A	Tang et al.	07-28-1998	
	A12	5,792,783	A	Tang et al.	08-11-1998	
	A13	5,880,141	A	Tang et al.	03-09-1999	
	A14	5,883,113	A	Tang et al.	03-16-1999	
	A15	5,883,116	A	Tang et al.	03-16-1999	
	A16	5,886,020	A	Tang et al.	03-23-1999	

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		Office <sup>3</sup>	Number <sup>4</sup>	Kind Code <sup>5</sup> (if known)				
	A17	WO	91/13055	A2	FARMITALIA CARLO ERBA SRL	09-05-1991		
	A18	WO	91/15495	A1	PFIZER INC.	10-17-1991		
	A19	WO	92/07830	A2	PFIZER INC.	05-14-1992		
	A20	WO	92/20642	A1	RHONEPOULENC RORER INTERNATIONAL	11-26-1992		
	A21	WO	92/21660	A1	PFIZER INC.	12-10-1992		
	A22	WO	93/23040	A1	MERCK & CO., INC.	11-25-1993		
	A23	WO	94/03427	A1	WARNER-LAMBERT COMPANY	02-17-1994		
	A24	WO	94/10202	A1	GENENTECH, INC.	05-11-1994		
	A25	WO	94/14808	A1	FARMITALIA CARLO ERBA SRL	07-07-1994		
	A26	WO	95/14667	A1	PFIZER INC.	06-01-1995		
	A27	WO	95/24190	A2	SUGEN, INC.	09-14-1995		
	A28	WO	96/00226	A1	PHARMACIA S.P.A.	01-04-1996		
	A29	WO	96/16964	A1	PHARMACIA S.P.A.	06-06-1996		
	A30	WO	96/22976	A1	PHARMACIA S.P.A.	08-01-1996		
	A31	WO	96/40116	A1	SUGEN, INC.	12-19-1996		
	A32	WO	98/07695	A1	SUGEN, INC.	02-26-1998		
	A33	WO	98/07835	A2	SUGEN, INC.	02-26-1998		
	A34	WO	98/45708	A1	SUGEN, INC.	10-15-1998		

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	A35	WO	98/50356	A1	SUGEN, INC.	11-12-1998		
	A36	WO	98/56376	A1	SUGEN, INC.	12-17-1998		
	A37	WO	99/10325	A1	GLAXO GROUP LIMITED	03-04-1999		
	A38	EP	0 252 713	B1	PFIZER INC.	01-13-1988		
	A39	EP	0 566 226	B1	ZENECA LIMITED	10-20-1993		
	A40	FR	1.398.224		IMPERIAL CHEMICAL INDUSTRIES LIMITED	05-07-1965		X
	A41	HU	3899/92		RICHTER GEDEON VEGYESZETI GYAR RT	12-10-1992		

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	A42	AKBASAK and SUNAR-AKBASAK, "Oncogenes: cause or consequence in the development of glial tumors," <u>J. Neurol. Sci.</u> 111:119-133 (1992)© Elsevier Science Publishers		
	A43	ANDREANI et al., "Synthesis and potential coanthracyclic activity of substituted 3-(5-imidazo[2,1-b]thiazolylmethylene)-2-indolinones," <u>Eur. J. Med. Chem.</u> 32:919-924 (1997)© Elsevier, Paris		
	A44	ANDREANI et al., "In Vivo Cardiotonic Activity of Pyridylmethylene-2-indolinones," <u>Arzneimittel-Forschung Drug Research</u> 48:727-729 (1998) ©		
	A45	ARTEAGA et al., "Blockade of the Type I Somatomedin Receptor Inhibits Growth of Human Breast Cancer Cells in Athymic Mice," <u>J. Clin. Invest.</u> 84:1418-1423 (1989) copyright The American Society for Clinical investigation, Inc.		

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	A46	ARVIDSSON et al., "Tyr-716 in the Platelet-Derived Growth Factor $\beta$ -Receptor Kinase Insert is Involved in GRB2 Binding and Ras Activation," <u>Molecular and Cellular Biology</u> 14:6715-6726 (1994) © The American Society for Microbiology	
	A47	BASERGA, "Oncogenes and the Strategy of Growth Factors," <u>Cell</u> 79:927-930 (1994) © Cell Press	
	A48	BASERGA, "The Insulin-like Growth Factor I Receptor: A Key to Tumor Growth?" <u>Cancer Research</u> 55:249-252 (1995)	
	A49	Beilstein Reg. No. 252929 (1998)	
	A50	BOLEN et al., "The Src family of tyrosine protein kinases in hemopoietic signal transduction," <u>FASEB J.</u> 6:3403-3409 (1992)	
	A51	BOLEN, "Nonreceptor tyrosine protein kinases," <u>Oncogene</u> 8:2025-2031 (1993) copyright MacMillan Press Ltd.	
	A52	BONNER et al., "Structure and Biological Activity of Human Homologs of the <i>raf/mil</i> Oncogene," <u>Molecular and Cellular Biology</u> 5:1400-1407 (1985) © The American Society for Microbiology	
	A53	BUZZETTI et al., "Cinnamamide Analogs as Inhibitors of Protein Tyrosine Kinases," <u>Il Farmaco</u> 48:615-636 (1993)	
	A54	CANCE et al., "Novel Protein Kinases Expressed in Human Breast Cancer," <u>Int. J. Cancer</u> 54:571-577 (1993) © Wiley-Liss, Inc.	

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	A55	CARPENEDO et al., "Identification and Measurement of Oxindole (2-Indolinone) in the Mammalian Brain and Other Rat Organs," <u>Analytical Biochemistry</u> 244:74-79 (1997) © Academic Press, Inc.	
	A56	CHEN et al., "Effects of 3,3-Dipyridylmethyl-1-Phenyl-2-Indolinone on $\gamma$ -Aminobutyric Acid Elicited Chloride Current of Snail Central Neuron," <u>Chinese Journal of Physiology</u> 40:149-156 (1997)	
	A57	CLAESSON-WELSH, "Signal Transduction by the PDGF Receptors," <u>Progress in Growth Factor Research</u> 5:37-54 (1994) © Elsevier Science Ltd.	
	A58	COPPOLA et al., "A Functional Insulin-Like Growth Factor I Receptor Is Required for the Mitogenic and Transforming Activities of the Epidermal Growth Factor Receptor," <u>Molecular and Cellular Biology</u> 14:4588-4595 (1994) © The American Society for Microbiology	
	A59	DAMIANI et al., "Inhibition of Copper-Mediated Low Density Lipoprotein Peroxidation by Quinoline and Indolinone Nitroxide Radicals," <u>Biochemical Pharmacology</u> 48:1155-1161 (1994) copyright Elsevier Science Ltd.	
	A60	DAVIS et al., "Synthesis and Microbiological Properties of 3-Amino-1-Hydroxy-2-Indolinone and Related Compounds," <u>Journal of Medicinal Chemistry</u> 16:1043-1045 (1973) © American Chemical Society	
	A61	DE VRIES et al., "The fms-Like Tyrosine Kinase, a Receptor for Vascular Endothelial Growth Factor," <u>Science</u> 255:989-991 (1992)	
	A62	DECKER and LOHMANN-MATTHES, "A quick and simple method for the quantitation of lactate dehydrogenase release in measurements of cellular cytotoxicity and tumor necrosis factor (TNF) activity," <u>J. Immunol. Methods</u> 15:61-69 (1988) copyright Elsevier	
	A63	DICKSON et al., "13. Tyrosine kinase receptor - nuclear protooncogene interactions in breast cancer," <u>Cancer Treatment Res.</u> 61:249-273 (1992) © Kluwer Academic Publishers	

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	A64	FANTL et al., "Distinct Phosphotyrosines on a Growth Factor Receptor Bind to Specific Molecules That Mediate Different Signaling Pathways," <u>Cell</u> 69:413-423 (1992) © Cell Press	
	A65	FENDLY et al., "Characterization of Murine Monoclonal Antibodies Reactive to Either the Human Epidermal Growth Factor Receptor or HER2/neu Gene Product," <u>Cancer Research</u> 50:1550-1558 (1990); © American Association for Cancer Research	
	A66	FERRARA and HENZEL, "Pituitary Follicular Cells Secrete a Novel Heparin-Binding Growth Factor Specific for Vascular Endothelial Cells," <u>Biochemical and Biophysical Research Communications</u> 161:851-858 (1989) © Academic Press, Inc.	
	A67	FINGL and WOODBURY, "Chapter 1 - General Principles," in <u>The Pharmacological Basis of Therapeutics</u> 5th edition, Goodman and Gilman editors, MacMillan Publishing Co., Inc., New York, pp. 1-46 (1975) © MacMillan Publishing Co. Inc.	
	A68	FLOEGE et al., "Factors involved in the regulation of mesangial cell proliferation <i>in vitro</i> and <i>in vivo</i> ," <u>Kidney International</u> 43:S47-S54 (1993) © International Society of Nephrology	
	A69	FOLKMAN and SHING, "Angiogenesis," <u>J. Biol. Chem.</u> 267:10931-10934 (1992) © The American Society for Biochemistry and Molecular Biology	
	A70	FOLKMAN, "Ch. 24. Angiogenesis," <u>Congress of Thrombosis and Haemostasis</u> (Verstraete et al., eds.) Leuven University Press, Leuven pp. 583-596 (1987)	
	A71	FOLKMAN, "Tumor Angiogenesis: Therapeutic Implications," <u>New England J. Medicine</u> 285:1182-1186 (1971)	
	A72	FOLKMAN, "What is the Evidence that Tumors are Angiogenesis Dependent?" <u>Journal of the National Cancer Institute</u> 82:4-6 (1990)	

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	A73	GAZIT et al., "Tyrphostins. 2. Heterocyclic and $\alpha$ -Substituted Benzylidenemalononitrile Tyrphostins as Potent Inhibitors of EGF Receptor and ErbB2/neu Tyrosine Kinases," <u>J. Med. Chem.</u> 34:1896-1907 (1991) copyright Am. Chem. Soc.	
	A74	GENNARO (editor), <u>Remington's Pharmaceutical Sciences</u> (1990) (TABLE OF CONTENTS ONLY)	
	A75	GOLDRING and GOLDRING, "Cytokines and Cell Growth Control," <u>Critical Reviews in Eukaryotic Gene Expression</u> 1:301-326 (1991)	
	A76	GRAZIANI et al., "Hepatocyte Growth Factor/Scatter Factor Stimulates the Ras-Guanine Nucleotide Exchanger," <u>The Journal of Biological Chemistry</u> 268:9165-9168 (1993) ©American Society for Biochemistry and Molecular Biology	
	A77	HONEGGER et al., "Point Mutation at the ATP Binding Site of EGF Receptor Abolishes Protein-Tyrosine Kinase Activity and Alters Cellular Routing," <u>Cell</u> 51:199-209 (1987) © Cell Press	
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	A81	KASHISHIAN and COOPER, "Phosphorylation Sites at the C-terminus of the Platelet-Derived Growth Factor Receptor Bind Phospholipase C $\gamma$ 1," <u>Molecular Biology of the Cell</u> 4:49-57 (1993) © The American Society for Cell Biology	

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				<b>Filing Date</b>	03/29/2001
Date Submitted:				<b>First Named Inventor</b>	Peng Cho TANG
				<b>Group Art Unit</b>	Unassigned
(use as many sheets as necessary)				<b>Examiner Name</b>	Unassigned
				<b>Attorney Docket Number</b>	034536-0906
Sheet	8	of	14		

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	A82	KASHISHIAN et al., "Phosphorylation sites in the PDGF receptor with different specificities for binding GAP and PI3 kinase <u>in vivo</u> ," <u>The EMBO Journal</u> 11:1373-1382 (1992)		
	A83	KATO et al., "Simultaneous Determination of Amfenac Sodium and its Metabolite (7-Benzoyl-2-Oxindole) in Human Plasma by High-Performance Liquid Chromatography," <u>Journal of Chromatography</u> 616:67-71 (1993) ©Elsevier Science		
	A84	KAZLAUSKAS et al., "The 64-kDa protein that associates with the platelet-derived growth factor receptor $\beta$ subunit via Tyr-1009 is the SH2-containing phosphotyrosine phosphatase Syp," <u>Proc. Natl. Acad. Sci. USA</u> 90:6939-6942 (1993)		
	A85	KENDALL and THOMAS, "Inhibition of vascular endothelial cell growth factor activity by an endogenously encoded soluble receptor," <u>Proc. Natl. Acad. Sci. USA</u> 90:10705-10709 (1993)		
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	A87	KINSELLA et al., "Protein Kinase C Regulates Endothelial Cell Tube Formation on Basement Membrane Matrix, Matrigel," <u>Exp. Cell Research</u> 199:56-62 (1992) © Academic Press, Inc.		
	A88	KLAGSBRUN and SOKER, "VEGF/VPF: the angiogenesis factor found?" <u>Current Biology</u> 3:699-702 (1993) ©Current Biology		
	A89	KOCH et al., "SH2 and SH3 Domains: Elements That Control Interactions of Cytoplasmic Signaling Proteins," <u>Science</u> 252:668-674 (1991)		
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	A91	KORC et al., "Overexpression of the Epidermal Growth Factor Receptor in Human Pancreatic Cancer Is Associated with Concomitant Increases in the Levels of Epidermal Growth Factor and Transforming Growth Factor Alpha," <u>J. Clin. Invest.</u> 90:1352-1360 (1992) copyright The American Society for Clinical Investigation, Inc.	
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	A97	MACAULAY et al., "Autocrine Function for Insulin-like Growth Factor I in Human Small Cell Lung Cancer Cell Lines and Fresh Tumor Cells," <u>Cancer Research</u> 50:2511-2517 (1990)	
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	A99	MILLAUER et al., "High Affinity VEGF Binding and Developmental Expression Suggest Flk-1 as a Major Regulator of Vasculogenesis and Angiogenesis," <u>Cell</u> 72:835-846 (1993) © Cell Press	

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	A100	MOHAMMADI et al., "Structures of the Tyrosine Kinase Domain of Fibroblast Growth Factor Receptor in Complex with Inhibitors," <u>Science</u> 276:955-960 (1997) © American Association for the Advancement of Science	
	A101	MORETO et al., "Study of the Laxative Properties of the Disodium Salt of the Sulfuric Diester of 3,3 Bis-(4-Hydroxyphenyl)-7-Methyl-2-Indolinone (DAN-603) in the Rat," <u>European Journal of Pharmacology</u> 36:221-226 (1976) ©North-Holland Publishing Company	
	A102	MORETO et al., "3,3-Bis-(4-Hydroxyphenyl)-7-Methyl-2-Indolinone (BHMI), the Active Metabolite of the Laxative Sulisatin," <u>Arzneimittel-Forschung Drug Research</u> 29:1561-1564 (1979)	
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	A104	MOSMANN, "Rapid Colorimetric Assay for Cellular Growth and Survival: Application to Proliferation and Cytotoxicity Assays," <u>J. Immunol. Methods</u> 65:55-63 (1983) copyright Elsevier Publishers B.V.	
	A105	NISHIMURA et al., "Two Signaling Molecules Share a Phosphotyrosine-Containing Binding Site in the Platelet-Derived Growth Factor Receptor," <u>Molecular and Cellular Biology</u> 13:6889-6896 (1993)	
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	A107	QUINN et al., "Fetal liver kinase 1 is a receptor for vascular endothelial growth factor and is selectively expressed in vascular endothelium," <u>Proc. Natl. Acad. Sci. USA</u> 90:7533-7537 (1993)	
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	A109	RYGAARD and POVLSEN, "Heterotransplantation of a Human Malignant Tumour to 'Nude' Mice," <u>Acta Path. Microbiol. Scand.</u> 77:758-760 (1969)	
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	A112	SHIBUYA et al., "Nucleotide sequence and expression of a novel human receptor-type tyrosine kinase gene (flt) closely related to the fms family," <u>Oncogene</u> 5:519-524 (1990)	
	A113	SHIRAIISHI et al., "Specific inhibitors of Tyrosine-Specific Protein Kinase, Synthetic 4-Hydroxycinnamamide Derivatives," <u>Biochemical and Biophysical Research Communications</u> 147:322-328 (1987) © Academic Press	
	A114	SINGH et al., "Indolinone Derivatives as Potential Antimicrobial Agents," <u>Zentralbl. Mikrobiol.</u> 144:105-109 (1989) copyright VEB Gustav Fischer Verlag Jena	
	A115	SINGH et al., "Synthesis and Anticonvulsant Activity of New 1-Substituted 1'-Methyl-3-Chloro-2-Oxospiro (Azetidin-3', 4-Indol-2' Ones)," <u>Bollettino Chimico Farmaceutico</u> 133:76-79 (1994)	
	A116	SINKULA, "Prodrug Approach in Drug Design," <u>Medicinal Chemistry</u> , Vol. 10, pp. 306-315, 1975, © Academic Press	
	A117	SLAMON et al., "Studies of the HER-2/neu Proto-oncogene in Human Breast and Ovarian Cancer," <u>Science</u> 244:707-712 (1989)	

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	A118	SOLDI et al., "Platelet-Activating Factor (PAF) Induces the Early Tyrosine Phosphorylation of Focal Adhesion Kinase (p125 <sup>FAK</sup> ) in Human Endothelial Cells," <u>Oncogene</u> 13:515-525 (1996) copyright Stockton Press		
	A119	SONGYANG et al., "SH2 Domains Recognize Specific Phosphopeptide Sequences," <u>Cell</u> 72:767-778 (1993) © Cell Press		
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	A121	SPADA, et al., "Small molecule inhibitors of tyrosine kinase activity," <u>Expert Opinion on Therapeutic Patents</u> 5:805-817 (1995) ©Ashley Publications		
	A122	SUN et al, "Synthesis and Biological Evaluations of 3-Substituted Indolin-2-ones: A Novel Class of Tyrosine Kinase Inhibitors That Exhibit Selectivity toward Particular Receptor Tyrosine Kinases," <u>J. Med. Chem.</u> 41:2588-2603 (1998) ©The American Chemical Society		
	A123	SUPERTI-FURGA et al., "A functional screen in yeast for regulators and antagonizers of heterologous protein tyrosine kinases," <u>Nature Biotech.</u> 14:600-605 (1996)		
	A124	SUPERTI-FURGA et al., "Csk inhibition of c-Src activity requires both the SH2 and SH3 domains of Src," <u>EMBO J.</u> 12:2625-2634 (1993) © Oxford University Press		
	A125	TAKANO et al., "Inhibition of angiogenesis by a novel diaminoanthraquinone that inhibits Protein Kinase C," <u>Mol. Bio. Cell</u> 4:358A at abstract no. 2076 (1993)		
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	A127	TRAXLER, "Protein tyrosine kinase inhibitors in cancer treatment," <u>Expert Opinion on Therapeutic Patents</u> 7(6):571-588 (1997) © Ashley Publications Ltd.		
	A128	TROST et al. (ed.), <u>Comprehensive Organic Synthesis, Selectivity, Strategy &amp; Efficiency in Modern Organic Chemistry</u> , 4:477-480 (1991), Elsevier Science Ltd.		
	A129	TSAI et al., "The Effect of 3,3-Di-Pyridyl Methyl-1-Phenyl-2-Indolinone on the Nerve Terminal Currents of Mouse Skeletal Muscles," <u>Neuropharmacology</u> 31:943-947 (1992) ©Pergamon Press		
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	A132	VAISMAN et al., "Characterization of the Receptors for Vascular Endothelial Growth Factor," <u>J. Biol. Chem.</u> 265:19461-19466 (1990) © The American Society for Biochemistry and Molecular Biology		
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	A135	WALKER et al., "Synthesis of New 3-(Pyridylmethylene)-, 3-(Pyridylmethyl)-, 3-(Piperidylmethyl)-, and 3-(β-Alkylaminoethyl)-2-indolinones. The Reduction of Isoindogenides, Nitro Compounds, and Pyridines in a Series of 2-Indolinones," <u>J. Med. Chem.</u> 8:626-637 (1965)		

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<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>				Application Number	
				09/819,698	
				Filing Date	
				03/29/2001	
				First Named Inventor	
		Peng Cho TANG			
Date Submitted:		Group Art Unit		Unassigned	
(use as many sheets as necessary)		Examiner Name		Unassigned	
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				034536-0906	

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Exami ner Initials *	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.		T <sup>6</sup>
	A136	WEIDNER et al., "Tumor Angiogenesis and Metastasis -- Correlation in Invasive Breast Carcinoma," <u>New England J. Medicine</u> 324:1-7 (1991) © Massachusetts Medical Society		
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	A138	ZAMAN et al., "Tyrosine Kinase Activity of Purified Recombinant Cytoplasmic Domain of Platelet-Derived Growth Factor $\beta$ -Receptor ( $\beta$ -PDGFR) and Discovery of a Novel Inhibitor of Receptor Tyrosine Kinases," <u>Biochemical Pharmacology</u> 57:57-64 (1999) ©Elsevier Science Inc.		
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